ORIGIN OF MECHANISM OF HEREDITY

CONTRIBUTIONS FROM THE HULL BOTANICAL LABORATORY 274

MERLE C. COULTER

The gross features of the mechanism of heredity have become features of general knowledge. The majority of biologists think of heredity in terms of determiners located upon the chromosomes. There are certain critical details of the mechanism, however, which still remain profoundly obscure. Little is known of the exact nature of the determiners themselves. The orderliness in the behavior of the determiners, that is, how they are "released" to express themselves only at the appropriate moments in the life history of the organism, seems not to have been clearly visualized. Finally, the possible origin of this mechanism of heredity is seldom even discussed. The present paper suggests, although only in a very brief and general way, certain answers to these questions.

It seems safe to assume that the most primitive organism lacked not only an organized nucleus, but even the components of a nucleus. A consideration of the activities of such an organism will reveal a suggestion as to the origin of the hereditary mechanism, provided, of course, that the assumptions are sound. The metabolism of this primitive organism, in certain fundamental features, will be similar to that of all organisms. Raw materials will be taken in and transformed to provide building materials and energy. If the raw materials be pure and the machinery of the protoplast perfect, this transformation will be complete, so that all the raw materials taken in will be transformed and used. Actually, however, the raw materials provided are never quite pure, and the machinery of the protoplast, although infinitely more efficient than any man-made machine, must be subject to certain flaws and frictions of its own. The transformation and use of materials, therefore, will not be complete; certain waste materials and by-products will remain. We are not concerned with the waste material; it is the fate of the by-products which is significant.

Certain of the by-products may be insignificant in their influence upon the protoplast. Others will undoubtedly be toxic in their effect, as many investigations upon auto-intoxication have gone to show. Primitive excretory systems, developed primarily for the disposal of waste materials, may remove a considerable part of these by-products. Thorough cleansing of the protoplast by this method, however, is impossible. Inevitably by-products will accumulate with the age of the organism. In fact age itself, in other than the purely chronological sense, is probably accounted for by this very accumulation of by-products. The toxic influence of these by-products will interfere with the efficient working of the machinery of the protoplast, and metabolism will be slowed down; hence "old age." Rejuvenescence occurs with cell division, because at cell division the protoplast is cleansed of many of these toxic by-products. This cleansing probably involves both physical and chemical forces. Physical reorganization at cell division will explain the exposure of these by-products; chemical oxidation will account for their removal (as toxins).

Again, were the machinery of this cleansing process a perfect one, rejuvenescence would be complete. Actually, however, the cleansing of the protoplast at cell division is not (or is not always) absolutely thorough. A few of the by-products pass over to the daughter protoplasts. The daughters, therefore, start life with a few by-products which the mother did not possess at the beginning of her life. Since these by-products are toxic and impair or retard metabolism, it is evident that the daughters are, at birth, slightly "older" than was the mother.

A series of repetitions of this performance through successive generations will have a cumulative effect. As a consequence, not only does the individual grow old through ontogeny, but, in a very real sense, the whole race is gradually aging through phylogeny. Evidence is not lacking that the higher organisms, cell for cell, have a lower rate of metabolism than do the more primitive ones. This is a statement of the quantitative effect of these by-products. It is their qualitative effect, however, that casts light upon the origin of the hereditary mechanism.

The by-products which originally accumulated in the protoplast were of various types. Some were very toxic, and these, if they were not immediately eliminated, resulted in the death of the organism. Others were less toxic, relatively more harmonious with the protoplast itself. These last, since they were not immediately fatal, stimulated an adaptive response on the part of the protoplast.

As to the general nature of this adaptive response, an important assumption must be made. Recent researches upon mammals have revealed in these organisms the power to develop antitoxins. The presence of a small quantity of toxin stimulates the organism to an adaptive response, the development of an antitoxin specific for the toxin present. This power is probably one of the fundamental characteristics of all protoplasm, being present even in the most primitive organisms.

Certain by-products in the primitive organism, only slightly toxic in their effect, stimulated it to produce an antibody. The protoplast is doubtless a colloidal system, and we may consider antibodies in the following light. The antibody counteracted the influence of the toxic by-product by insulating it from contact with the protoplast. Antibodies were probably developed most successfully for those by-products which were the least toxic in their effect. These by-products then became insulated by the antibodies. This insulation was significant not only in cutting off the influence of the by-product upon the protoplast, but in another respect also. At cell division this by-product, even though exposed, is not oxidized because of the protection afforded by the antibody which insulates it. It is probably this mechanism, for the most part, which accounts for the fact that some of the by-products are passed on to the daughter protoplasts, as mentioned before. These by-products are the primitive bearers of hereditary characters. The program carried out by the primitive hereditary mechanism is as follows.

The life of the primitive organism, like that of all organisms, involves a series of reactions. Early in the life of the organism there is present a certain reaction system, characterized by certain physical and chemical conditions. For a time the reaction system

as a whole maintains a sort of equilibrium, in which only reactions of a certain type are possible. This may be referred to as the *A* equilibrium. Inevitably, through the accumulation of certain materials, the *A* equilibrium will be upset. After a period of readjustment, the *B* equilibrium will succeed; this will be followed by the *C* equilibrium, and so on. The total number of distinct equilibria in the life program of any organism probably is in rough proportion to phylogenetic age.

Taking as an example the *X* equilibrium, certain questions may be considered. What is it that accounts for the existence of the *X* equilibrium? It is the inevitable result of reactions which took place during the *W* equilibrium. The *W* equilibrium may be similarly accounted for by the previous existence of the *V* equilibrium. The program is an inevitable one, and will be followed during each generation.

Under conditions imposed by the *X* equilibrium, only reactions of a certain type are possible, and these may be referred to as the x reactions. A number of x reactions are possible, x_1, x_2, x_3, etc. Chance conditions (environment, directly or indirectly) will determine which of these will take place. Whichever takes place, there will result a by-product, and this by-product will be of the x type. Even more specific than this, the x_3 reaction will result in and be characterized by the x_3 by-product. As the existence of the *X* equilibrium was inevitable, there will inevitably be laid down one of the x type of by-products. Since, however, it was chance which specifically selected the x_3 reaction, this same chance is indirectly responsible for the by-product x_3, rather than x_1, x_2, or any of the other possibilities.

The by-product x_3 will exist in an active state and exert some influence upon the protoplast so long as the *X* equilibrium continues. The eventual disappearance of the *X* equilibrium will be accompanied and characterized by the insulation of by-product x_3 by means of a specific antibody which has been developed by the protoplast. The *Y* equilibrium will follow; and, just as the *X* equilibrium was characterized by the free active existence of by-product x_3, one of the characteristics of the *Y* equilibrium will be the existence of x_3 in an insulated inactive condition. The by-

product x_3, insulated by its antibody, will pass on at cell division to the daughter protoplast. Early in the life of the daughter there must exist an A equilibrium. The inevitable program will then be followed, until finally the X equilibrium is reached. A very critical assumption is made at this point. The insulation of x_3 by its antibody is a phenomenon of colloidal chemistry. Similar colloidal reactions are known to be reversible. The formation of the antibody for x_3 took place at the inception of the Y equilibrium, which was characterized by the effective insulation of x_3. The X equilibrium, however, which now recurs during the following generation, is conducive to the free and active existence of any by-product of the x type. When the X equilibrium is reached in the life of the daughter protoplast, therefore, a dissolution of the antibody will occur and x_3 will be released.

With the X equilibrium now in existence, it is certain that reactions of the x type will take place. Which one of the possible x reactions occurred was in the first generation a matter of chance. In the present instance, however, the presence of by-product x_3 will exert a determining influence. The result, eliminating external stimuli of an unusual intensity, will be that the x_3 reaction and the x_3 by-product again stimulate the protoplast in a characteristic manner, developing in the daughter the same characteristic that was present at a similar stage in the life of the mother.

This theory accounts for the origin of the hereditary mechanism in terms of by-products and antibodies which insulate them. These various antibodies must form an important constituent of "modern" chromosomes, but there must also be present some more stable and homogeneous framework.

The release of the determiners (by-products) at the appropriate moment is referred to phenomena of colloidal chemistry. It is an open question whether this release is reflected by visible changes in the chromosomes. If so, a given locus on a chromosome should be seen in a loose or "open" condition only during a brief phase of the life history. No doubt this point would be hopeless to ascertain in any very accurate way.

As for the determiners themselves, these are visualized as by-products of metabolism, chemically active substances. The

reaction system (for example, X equilibrium), which arises as the result of an inevitable sequence of events, determines what general type of reaction shall take place at a given phase in the life history. The by-product (for example, x_3) merely decides which of a number of possible reactions within this general type shall be the one chosen.

The origin of a given by-product was accounted for by chance environmental conditions. The environment referred to may well have been the external environment in the case of the simpler organisms, but must be the internal environment in the more complex. This seems also to provide sufficient basis to explain the small degree of inheritance of acquired characters that has been said to take place.

University of Chicago